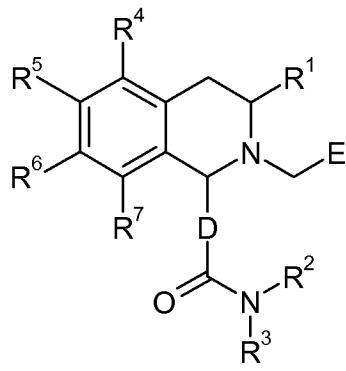


In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (original) A compound of formula I, a pharmaceutically acceptable salt thereof, diastereomers, enantiomers, or mixtures thereof:



I

wherein

R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl;

R⁴, R⁵, R⁶ and R⁷ are independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-l-oxy, C₃₋₆heterocycl-l-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or any two adjacent groups selected from R⁴, R⁵, R⁶ and R⁷ form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-l-oxy, C₃₋₆heterocycl-l-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl;

E is a 5-membered heterocycl optionally substituted with one or more groups selected from halogen, C₁₋₆alkyl, -C(=O)-O-C₁₋₆alkyl, C₆₋₁₀aryl, C₆₋₁₀aryl-C₁₋₄alkyl, and C₆₋₁₀aryl-S(=O)₂-; and

D is a divalent group comprising a benzene ring.

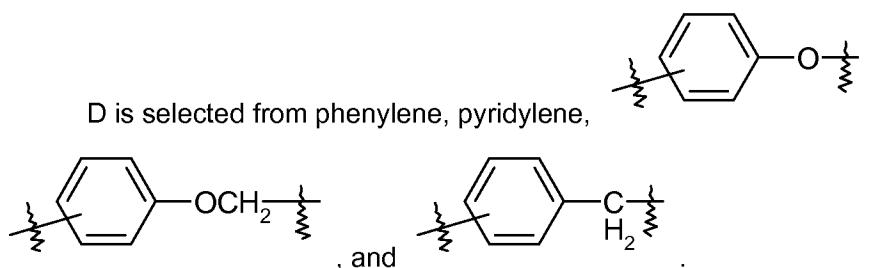
2. (original) A compound according to claim 1, wherein

R¹ is selected from -H and C₁₋₃alkyl;

R² and R³ are independently C₁₋₃alkyl;

R^4 , R^5 , R^6 and R^7 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, $C_{1-6}alkyl$, phenyl, $C_{1-6}alkoxy$, $C_{3-6}cycloalkoxy$, tetrahydropyranloxy, pyridinyloxy, morpholinyloxy, tetrahydropyranyl- $C_{1-4}alkoxy$, pyridinyl- $C_{1-4}alkoxy$, morpholinyl- $C_{1-4}alkoxy$, phenoxy, benzyloxy, $C_{1-6}alkyl-S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, $C_{1-3}alkyl-NH-S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$; or any two adjacent groups selected from R^4 , R^5 , R^6 and R^7 form a divalent group selected from $-O-CH_2-O-$ and $-O-CH_2-CH_2-O-$, wherein said $C_{1-6}alkyl$, phenyl, $C_{1-6}alkoxy$, $C_{3-6}cycloalkoxy$, tetrahydropyranloxy, pyridinyloxy, morpholinyloxy, tetrahydropyranyl- $C_{1-4}alkoxy$, pyridinyl- $C_{1-4}alkoxy$, morpholinyl- $C_{1-4}alkoxy$, phenoxy, benzyloxy, $C_{1-6}alkyl-S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, $C_{1-3}alkyl-NH-S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen, methoxy, $-OH$, $-NO_2$, and $C_{1-3}alkyl$;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more groups selected from halogen, $C_{1-4}alkyl$, $-C(=O)-O-C_{1-3}alkyl$, phenyl, benzyl, and benzenesulfonyl; and



3. (original) A compound according to claim 1, wherein

R^1 is selected from $-H$ and methyl;

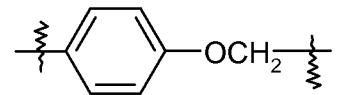
R^2 and R^3 are selected from ethyl and isopropyl;

R^4 , R^5 and R^6 are independently selected from $-H$, $-OH$, halogen, $-NO_2$, $C_{1-6}alkyl$, phenyl, $C_{1-6}alkoxy$, $C_{3-6}cycloalkoxy$, tetrahydropyranloxy, pyridinyloxy, morpholinyloxy, tetrahydropyranyl- $C_{1-4}alkoxy$, pyridinyl- $C_{1-4}alkoxy$, morpholinyl- $C_{1-4}alkoxy$, phenoxy, benzyloxy, $C_{1-6}alkyl-S(=O)_2-O-$, phenyl- $S(=O)_2-O-$, $C_{1-3}alkyl-NH-S(=O)_2-O-$, and $(C_{1-3}alkyl)_2N-S(=O)_2-O-$; or any two adjacent groups selected from R^4 , R^5 and R^6 form $-O-CH_2-O-$, wherein said phenoxy, benzyloxy, and phenyl- $S(=O)_2-O-$ are optionally substituted with one or more groups selected from halogen and methoxy;

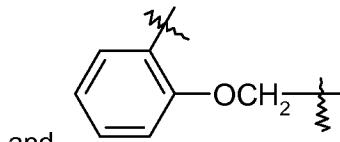
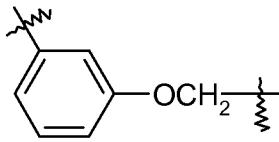
R^7 is selected from $-H$ and $C_{1-3}alkoxy$;

E is selected from furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl, wherein said furyl, thienyl, imidazolyl, pyrazolyl, and thiazolyl are optionally substituted with one or more

groups selected from halogen, C₁₋₄alkyl, -C(=O)-O-C₁₋₃alkyl, phenyl, benzyl, and benzenesulfonyl; and



D is selected from *para*-phenylene, *para*-benzylene,



, and

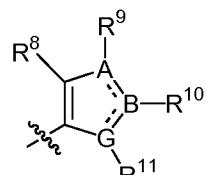
4. (original) A compound according to claim 1, wherein

R¹ is selected from -H and methyl;

R² and R³ are ethyl;

R⁴ is selected from -H, NO₂ and methoxy, R⁵ is selected from -H, -Br, -F, -OH, methoxy, methylsulfonyloxy, N,N-dimethylsulfamidoxy, and R⁶ is selected from -H, -OH, -NO₂, methoxy, ethoxy, isopropoxy, neopentyloxy, cyclobutoxy, 4-tetrahydro-2H-pyranloxy, 2-(4-morpholino)ethoxy, benzyloxy, phenoxy, 4-fluorophenoxy, 3-methoxyphenoxy, 4-methoxyphenoxy, 3-pyridinyloxy, methanesulfonyloxy, benzenesulfonyloxy, dimethylsulfamidoxy; or any two adjacent groups selected from R⁴, R⁵ and R⁶ form -O-CH₂-O-;

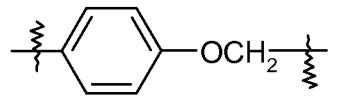
R⁷ is selected from -H and methoxy;



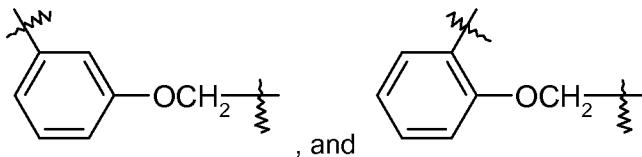
E is

, wherein A and B are independently selected from C, N and S, and G is selected from C, N, O and S with a proviso that at least one of A, B and G is C, at most one of A, B and G is S and one of the bonds between A and B, and between B and G is a double bond;

wherein R⁸ is selected from -H, -Cl, methyl, -CO₂Me and phenyl; R⁹ is selected from -H and methyl; R¹⁰ is selected from -H, methyl, n-butyl and phenyl; R¹¹ is selected from -H, methyl, benzyl and benzenesulfonyl.



D is selected from *para*-phenylene, *para*-benzylene,



5. (original) A compound selected from:

COMPOUND 12.1.1: N,N-Diethyl-2-{{2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}benzamide

COMPOUND 12.1.2: 2-{{6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.3: N,N-Diethyl-3-{{2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}benzamide

COMPOUND 12.1.4: 3-{{6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.5: N,N-Diethyl-4-{{2-(2-furylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}benzamide

COMPOUND 12.1.6: 4-{{6,7-Dimethoxy-2-(thien-3-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.7: 2-{{6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)methoxy}-N,N-diethylbenzamide

COMPOUND 12.1.8: 4-{{6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl}-N,N-diethylbenzamide

COMPOUND 12.1.9: 4-{{6,7-Dimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.10: N,N-Diethyl-4-{{6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.11: N,N-Diethyl-4-{{7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.12: N,N-Diethyl-4-{{2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.13: 4-{{2-[(2-Butyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.14: 4-{{2-[(2-Butyl-4-chloro-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.15: 4-{6,7-Dimethoxy-2-[(2-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.16: 4-{6,7-Dimethoxy-2-[(3-phenyl-1H-pyrazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.17: 4-(6,7-Dimethoxy-2-[(1-phenylsulfonyl)-1H-pyrrol-2-yl]methyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 12.1.18: N,N-Diethyl-4-{2-[(2-ethyl-4-methyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.19: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.20: 4-{5,8-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.21: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 12.1.22: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.23: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.24: 4-{6,7-Dimethoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.25: N,N-Diethyl-4-{6-methoxy-2-[(5-phenyl-2-furyl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.26: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.27: N,N-Diethyl-4-{7-hydroxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.28: 4-{2-[(1-Benzyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.29: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.30: 4-{6,7-Dimethoxy-2-[(1-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.31: 4-{6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}methoxy)-N,N-diethylbenzamide

COMPOUND 12.1.32: 4-{(6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl}-N,N-diethylbenzamide

COMPOUND 12.1.33: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.34: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl methanesulfonate

COMPOUND 12.1.35: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.36: 1-{4-[(Diethylamino)carbonyl]phenyl}-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-6-yl dimethylsulfamate

COMPOUND 12.1.37: 4-{2-[(2,5-Dimethyl-1,3-thiazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.38: 4-{6,7-Dimethoxy-2-[(2-phenyl-1,3-thiazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.39: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.40: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(2-morpholin-4-ylethoxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.41: 4-{7-Ethoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.42: N,N-Diethyl-4-{7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.43: N,N-Diethyl-4-{6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.44: N,N-Diethyl-4-{7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.45: Methyl 5-{{1-4-[(diethylamino)carbonyl]phenyl}-6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)methyl}-1H-imidazole-4-carboxylate

COMPOUND 12.1.46: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl methanesulfonate

COMPOUND 12.1.47: N,N-Diethyl-4-{6-[(4-methyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.48: N,N-Diethyl-4-{6-[(2-phenyl-1H-imidazol-5-yl)methyl]-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl}benzamide

COMPOUND 12.1.49: 4-{6-Bromo-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.50: 4-{6-Bromo-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.51: 4-{6,7-Dimethoxy-3-methyl-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.52: N,N-Diethyl-4-[2-(1H-imidazol-5-ylmethyl)-6,7-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.53: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-7-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.54: N,N-Diethyl-4-{6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-5-nitro-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.55: N,N-Diethyl-4-{7-[(4-methyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.56: N,N-Diethyl-4-{7-[(2-phenyl-1H-imidazol-5-yl)methyl]-6,7,8,9-tetrahydro[1,3]dioxolo[4,5-f]isoquinolin-6-yl}benzamide

COMPOUND 12.1.57: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.58: N,N-Diethyl-4-{5,6,7-trimethoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.59: 4-{7-(Cyclobutyloxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 12.1.60: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(neopentyloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 12.1.61: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.62: N,N-Diethyl-4-{6-fluoro-7-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 12.1.63: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl dimethylsulfamate

COMPOUND 13.1.1: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(tetrahydro-2H-pyran-4-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 14.1.1: N,N-Diethyl-4-{6-methoxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.2: N,N-Diethyl-4-{6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.3: N,N-diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.4: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.5: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 14.1.6: N,N-Diethyl-4-[6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-(pyridin-3-yloxy)-1,2,3,4-tetrahydroisoquinolin-1-yl]benzamide

COMPOUND 15.1.1: 4-{7-(Benzylxy)-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 16.4.1: N,N-Diethyl-4-{6-methoxy-7-(3-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.2: N,N-Diethyl-4-{6-methoxy-7-(4-methoxyphenoxy)-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 16.4.3: 1-{4-[(Diethylamino)carbonyl]phenyl}-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-7-yl benzenesulfonate

COMPOUND 17.1.1: 4-{6,7-Dihydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 17.1.2: N,N-Diethyl-4-{6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.3: N,N-Diethyl-4-{7-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.4: N,N-Diethyl-4-[1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinolinyl]benzamide

COMPOUND 17.1.5: N,N-Diethyl-4-{7-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.6: N,N-Diethyl-4-{6-hydroxy-7-phenoxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.7: N,N-Diethyl-4-{6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-7-phenoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.8: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(2-phenyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 17.1.9: N,N-Diethyl-4-{7-(4-fluorophenoxy)-6-hydroxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}benzamide

COMPOUND 18.1.1: 4-{2-[(1,4-Dimethyl-1H-imidazol-5-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 18.1.2: 4-{2-[(1,5-Dimethyl-1H-imidazol-4-yl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 19.1.1: 4-{7-Ethoxy-6-methoxy-2-[(5-methyl-1H-imidazol-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-N,N-diethylbenzamide

COMPOUND 20.1.1: 4-((1S)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 20.2.1: 4-((1R)-6,7-Dimethoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)-N,N-diethylbenzamide

COMPOUND 20.1.2: N,N-Diethyl-4-((1S)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.2: N,N-Diethyl-4-((1R)-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.3: N,N-Diethyl-4-((1S)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.3: N,N-Diethyl-4-((1R)-6-hydroxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.4: N,N-Diethyl-4-((1S)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.4: N,N-Diethyl-4-((1R)-7-isopropoxy-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.5: N,N-Diethyl-4-((1S)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.5: N,N-Diethyl-4-((1R)-7-isopropoxy-6-methoxy-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.6: N,N-Diethyl-4-((1S)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.2.6: N,N-Diethyl-4-((1R)-6-methoxy-7-(2-morpholin-4-ylethoxy)-2-[(2-phenyl-1H-imidazol-5-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-yl)benzamide

COMPOUND 20.1.7: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 20.2.7: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-methoxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 20.1.8: N,N-Diethyl-4-[(1S)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide

COMPOUND 20.2.8: N,N-Diethyl-4-[(1R)-1,2,3,4-tetrahydro-6-hydroxy-2-[(4-methyl-1H-imidazol-5-yl)methyl]-1-isoquinoliny]-benzamide;

and pharmaceutically acceptable salts thereof.

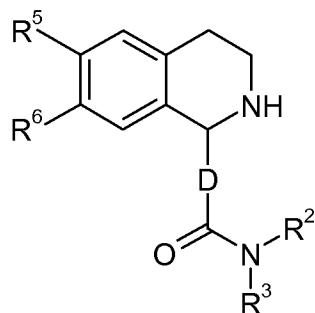
6-7. (cancelled)

8. (currently amended) A pharmaceutical composition comprising a compound according to claim 1 ~~any one of claims 1-5~~ and a pharmaceutically acceptable carrier.

9. (currently amended) A method for the therapy of pain in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to any one of claims 1-5 claim 1.

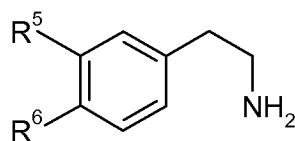
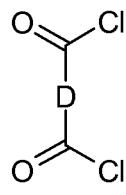
10. (currently amended) A method for the therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to any one of claims 1-5 claim 1.

11. (original) A process for preparing a compound of formula II,



II

comprising of the step of reacting a compound of formula III with a compound of formula IV in the presence of HNR^2R^3 :



III

IV

,

wherein

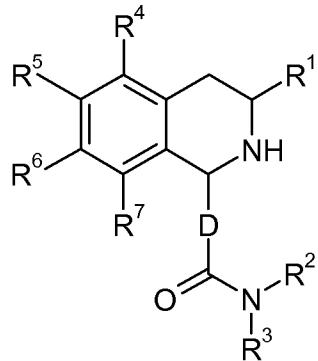
R^2 and R^3 are independently selected from $-\text{H}$ and $\text{C}_{1-6}\text{alkyl}$;

R^5 and R^6 are independently selected from $-\text{H}$, $-\text{OH}$, halogen, $-\text{NO}_2$, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{6-10}\text{aryl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{3-6}\text{cycloalkoxy}$, $\text{C}_{3-6}\text{heterocycl-oxy}$, $\text{C}_{3-6}\text{heterocycl-C}_{1-4}\text{alkoxy}$, $\text{C}_{6-10}\text{aryl-oxy}$, $\text{C}_{6-10}\text{aryl-C}_{1-4}\text{alkoxy}$, $\text{C}_{1-6}\text{alkyl-S(=O)}_2\text{O-}$, $\text{C}_{6-10}\text{aryl-S(=O)}_2\text{O-}$, $\text{C}_{1-6}\text{alkyl-NH-S(=O)}_2\text{O-}$,

and $(C_{1-6}\text{alkyl})_2\text{N-S}(=\text{O})_2\text{-O-}$; or R^5 and R^6 together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said $C_{1-6}\text{alkyl}$, $C_{6-10}\text{aryl}$, $C_{1-6}\text{alkoxy}$, $C_{3-6}\text{cycloalkoxy}$, $C_{3-6}\text{heterocycl-}C_{1-4}\text{alkoxy}$, $C_{6-10}\text{aryl-}O$, $C_{6-10}\text{aryl-}C_{1-4}\text{alkoxy}$, $C_{1-6}\text{alkyl-}S(=\text{O})_2\text{-O-}$, $C_{6-10}\text{aryl-}S(=\text{O})_2\text{-O-}$, $C_{1-6}\text{alkyl-}NH\text{-}S(=\text{O})_2\text{-O-}$, and $(C_{1-6}\text{alkyl})_2\text{N-S}(=\text{O})_2\text{-O-}$ are optionally substituted with one or more groups selected from halogen, $C_{1-3}\text{alkoxy}$, $-OH$, $-NO_2$, $C_{1-3}\text{alkyl}$, $-NH_2$, and $-CO_2\text{-}C_{1-3}\text{alkyl}$; and

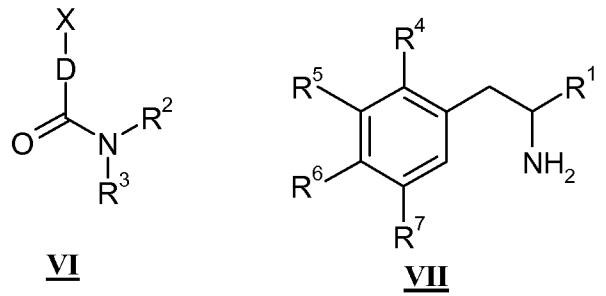
D is a divalent group comprising a benzene ring.

12. (original) A process for preparing a compound of formula V,



V

comprising of the step of reacting a compound of formula VI with a compound of formula VII in the presence of an acid catalyst:



wherein

X is selected from $-\text{CH}(\text{OEt})_2$, $=\text{CHOMe}$ and $-\text{CHO}$;

R^1 is selected from $-\text{H}$ and $C_{1-6}\text{alkyl}$;

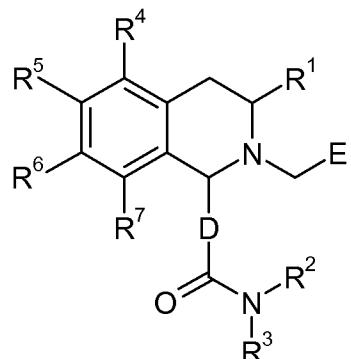
R^2 and R^3 are independently selected from $-\text{H}$ and $C_{1-6}\text{alkyl}$;

R^4 , R^5 , R^6 and R^7 are independently selected from $-\text{H}$, $-OH$, halogen, $-NO_2$, $C_{1-6}\text{alkyl}$, $C_{6-10}\text{aryl}$, $C_{1-6}\text{alkoxy}$, $C_{3-6}\text{cycloalkoxy}$, $C_{3-6}\text{heterocycl-}C_{1-4}\text{alkoxy}$, $C_{6-10}\text{aryl-}O$, $C_{6-10}\text{aryl-}C_{1-4}\text{alkoxy}$, $C_{1-6}\text{alkyl-}S(=\text{O})_2\text{-O-}$, $C_{6-10}\text{aryl-}S(=\text{O})_2\text{-O-}$, $C_{1-6}\text{alkyl-}NH\text{-}S(=\text{O})_2\text{-O-}$, and $(C_{1-6}\text{alkyl})_2\text{N-S}(=\text{O})_2\text{-O-}$; or any two adjacent groups selected from R^4 , R^5 , R^6 and R^7 form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I,

wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl; and

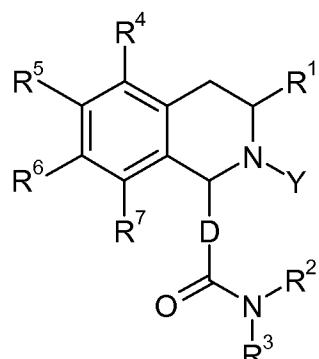
D is a divalent group comprising a benzene ring.

13. (original) A process for preparing a compound of formula I,



I

comprising: reacting a compound of formula VIII with E-CHO:



VIII

wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl;

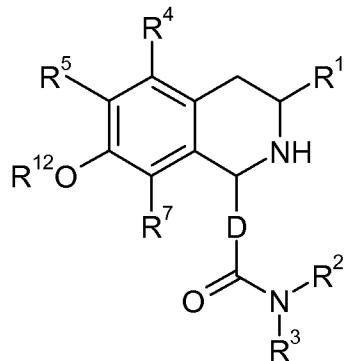
R⁴, R⁵, R⁶ and R⁷ are independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or any two adjacent groups selected from R⁴, R⁵, R⁶ and R⁷

form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C_{1-6} alkyl, C_{6-10} aryl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{3-6} heterocycl-*oxy*, C_{3-6} heterocycl- C_{1-4} alkoxy, C_{6-10} aryl-*oxy*, C_{6-10} aryl- C_{1-4} alkoxy, C_{1-6} alkyl- $S(=O)_2$ -*O*-, C_{6-10} aryl- $S(=O)_2$ -*O*-, C_{1-6} alkyl- NH - $S(=O)_2$ -*O*-, and $(C_{1-6}$ alkyl) $_2$ N - $S(=O)_2$ -*O*- are optionally substituted with one or more groups selected from halogen, C_{1-3} alkoxy, -OH, -NO₂, C_{1-3} alkyl, -NH₂, and -CO₂- C_{1-3} alkyl;

E is a 5-membered heterocycl optionally substituted with one or more groups selected from halogen, C_{1-6} alkyl, -C(=O)-O- C_{1-6} alkyl, C_{6-10} aryl, C_{6-10} aryl- C_{1-4} alkyl, and C_{6-10} aryl- $S(=O)_2$ -; and

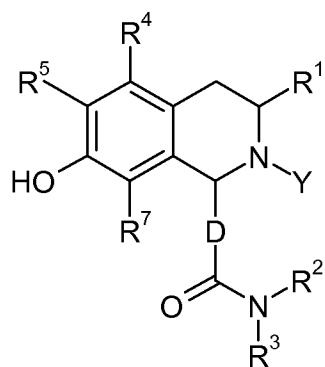
D is a divalent group comprising a benzene ring.

14. (original) A process for preparing a compound of formula IX,



IX

comprising: reacting a compound of formula X with R¹²-OH or R¹²-B(OH)₂:



X ,

wherein

Y is selected from -H and -C(=O)-O-t-butyl;

R¹² is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-6} heterocycl- C_{1-4} alkyl, C_{6-10} aryl, and C_{3-6} heteroaryl, wherein said C_{6-10} aryl, C_{3-6} heterocycl and C_{3-6} heteroaryl

are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂ and -CO₂-C₁₋₃alkyl; and

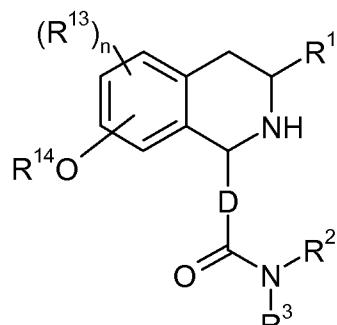
R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl;

R⁴, R⁵, and R⁷ are independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-
oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or R⁴ and R⁵ together form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-
oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl; and

D is a divalent group comprising a benzene ring.

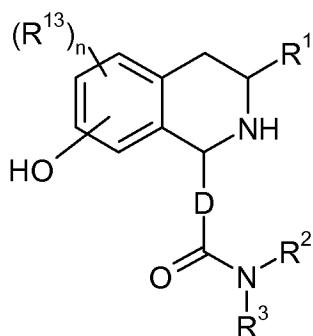
15. (original) A process for preparing a compound of formula XI,



comprising:

reacting a compound of formula XII with NsCl, NsBr, or (CF₃CO)₂O to protect the =NH group of formula XI;

reacting the protected compound with R¹⁴-Y¹ followed by deprotecting the =NH group;

**XII**

wherein

n is 0, 1, 2 or 3;

each R¹³ is independently selected from -H, -OH, halogen, -NO₂, C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O-; or any two adjacent R¹³ form a portion of a 5 or 6-membered ring that fused with the benzene ring of formula I, wherein said C₁₋₆alkyl, C₆₋₁₀aryl, C₁₋₆alkoxy, C₃₋₆cycloalkoxy, C₃₋₆heterocycl-oxy, C₃₋₆heterocycl-C₁₋₄alkoxy, C₆₋₁₀aryl-oxy, C₆₋₁₀aryl-C₁₋₄alkoxy, C₁₋₆alkyl-S(=O)₂-O-, C₆₋₁₀aryl-S(=O)₂-O-, C₁₋₆alkyl-NH-S(=O)₂-O-, and (C₁₋₆alkyl)₂N-S(=O)₂-O- are optionally substituted with one or more groups selected from halogen, C₁₋₃alkoxy, -OH, -NO₂, C₁₋₃alkyl, -NH₂, and -CO₂-C₁₋₃alkyl;;

Y¹ is halogen;

R¹⁴ is selected from C₁₋₆alkyl-S(=O)₂-, C₆₋₁₀aryl-S(=O)₂-, C₁₋₆alkyl-NH-S(=O)₂-, and (C₁₋₆alkyl)₂N-S(=O)₂-;

R¹ is selected from -H and C₁₋₆alkyl;

R² and R³ are independently selected from -H and C₁₋₆alkyl; and

D is a divalent group comprising a benzene ring.

16. (new) A method for the therapy of anxiety in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to claim 1.